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John F. Smith MD 1/27/96
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INTRODUCTION

Improved detection has resulted in a reduction in the average size of invasive breast cancers in mammogram-screened populations during the past 10-15 years. Data from our Institution is shown below in Table I. Note that small primary invasive breast cancers, usually defined as tumors less than 1 cm. in size, now account for almost one-third (30.7%) of breast cancers at our University Hospital. In 1983 such tumors accounted for only 6.4% of invasive cancers.

TABLE I

SIZE OF INVASIVE CARCINOMA OF THE BREAST AT TISCH HOSPITAL,
NYU MEDICAL CENTER BY YEAR

	<u>1983</u>	<u>1987</u>	<u>1991</u>	<u>1994</u>
# cases*	78	96	91	101
mean size (cm.)	2.12	1.97	1.63	1.58
# (%) < 1 cm.	5 (6.4)	15 (15.6)	23 (25.3)	31 (30.7)
# (%) < 0.5 cm.	2 (2.5)	2 (2.1)	10 (11.0)	14 (13.9)

*Data spans the 6 month period January to June for each year.

Additionally, the precursor lesions of invasive carcinoma, namely ductal carcinoma in situ and florid hyperplasia, previously rarely encountered in the absence of an associated invasive carcinoma, are now frequently seen as the sole pathology in surgical biopsy material.

Many cancer research techniques require the use of fresh tissue. In the case of most small breast cancers, in situ cancers and precancerous lesions no tissue can be spared for research purposes since the entire lesion is used for clinically necessary analyses (precise histologic classification, hormone receptors, cell cycle, and other assays) which determine further patient care decisions (Ref. 1). Therefore, human breast cancer research that requires fresh tissue has, to date, relied on samples of large/advanced cancers from which pieces could be spared for research purposes without compromising patient care.

We proposed that fine needle aspiration and tissue imprints/touch preps, two techniques increasingly used for clinical diagnosis, could be used to acquire small specimens of early cancers and precancers of the breast, without compromising patient care. Such specimens could provide researchers with new material for studies of human breast carcinogenesis.

METHODS

A breast cancer resource technician was hired and trained by the Principal Investigator in the acquisition of material from various types of breast tissue surgical specimens with clinically and mammographically defined lesions.

Capital items, in particular a deep freezer and a personal computer, were purchased, as well as necessary small equipment and supplies.

Tissue and cell banking protocols were established.

Record-keeping was established using an IBM-compatible PC and "Microsoft Access 2.1", a relational database in a customized format.

For the past year we have been collecting samples of small invasive breast cancers and precursor lesions using fine needle aspiration and imprint/scrape cytology preparations. We have also, of course, collected samples of larger primary as well as metastatic tumors and normal breast tissue (paired samples), using conventional tissue banking methods.

The availability of early breast cancers and precursor lesions has been made known to the NYU research community through the Kaplan Comprehensive Cancer Center's quarterly publication, "Lab Notes", pages 2-3 (see Appendix).

RESULTS

During the period 12/1/94 - 11/30/95 breast tissue samples from 430 cases have been banked and entered into our database. The breakdown by histopathologic type of lesion is shown in Table II.

The banked material is classified according to the type(s) of available sample(s) in Table III. Note that in this table the number of samples exceeds the number of cases because a single case often yielded more than one sample type.

TABLE II

CASES FROM TISCH AND BELLEVUE HOSPITALS, NYU MEDICAL CENTER,
THAT ARE BANKED IN THE BREAST TISSUE RESOURCE,
BY HISTOPATHOLOGIC DIAGNOSIS

	<u>Tisch</u>	<u>Bellevue</u>	<u>Total</u>
Invasive Ductal Carcinoma	111	7	118
Invasive Lobular Carcinoma	15	1	16
In-Situ Ductal Carcinoma	51	4	55
In-Situ Lobular Carcinoma	11	0	11
Secondary Carcinoma	44	7	25
Fibroadenoma	40	8	48
Fibrocystic - Proliferative	77	9	86
Normal/Non Proliferative Fibrocystic, Other	<u>62</u>	<u>9</u>	<u>71</u>
TOTAL	411	45	456

TABLE III

BANKED SAMPLES OF BREAST CANCER AND PRECANCEROUS LESIONS FROM
TISCH AND BELLEVUE HOSPITALS, NYU MEDICAL CENTER, BY SAMPLE TYPE

	<u>Tisch</u>	<u>Bellevue</u>	<u>Total</u>
Imprints/touch preps	332	35	367
Aspirated cells	135	14	149
Snap frozen tissue fragments	<u>197</u>	<u>36</u>	<u>233</u>
TOTAL	664	85	749

CONCLUSIONS

Our goals in terms of amount of material acquired and the range of pathologic types of breast diseases, have been met for the first year of collection.

Changes and future work: Since January 1, 1996 we have added to the types of specimens collected samples of normal (non-tumoral) lymph nodes from patients with breast cancer who have lymph node resections. One-third to one-half of a single grossly negative lymph node is acquired, under the direct supervision of the responsible attending pathologist. This material is of potential use in investigations of immune responses in tumor-draining lymph nodes.

To stimulate utilization of our resource, applications were requested for pilot projects in collaborative research on breast cancer to be funded by the Kaplan Comprehensive Cancer Center Breast Cancer Program Planning Grant, 5R21 CA66229-02, from the National Cancer Institute. Eleven proposals were submitted, of which three were funded (one year grants for 1996):

- 1) Cowin, P. - "The role of plakoglobin in breast cancer."
- 2) Sun, X.-H. - "The role of ID proteins in breast cancer."
- 3) Perle, M.A. and Illei, P. - "Interphase cytogenetic study of chromosome 7, 18, 20 and X in mammogram detected atypical ductal hyperplasia and ductal carcinoma in situ."

In collaboration with the NYU Grants Administration and Research Services an updated listing of all material available in the Breast Cancer Resource is being distributed to all NYU investigators who hold breast cancer grants or will receive breast cancer grants in the future.

REFERENCE

- 1) Moezzi, M., Melamed, J., Vamvakas, E., Inghirami, G., Mitnick, J., Quish, A., Bose, S., Roses, D., Harris, M., and Feiner, H. Morphologic and biologic characteristics of mammogram-detected invasive breast cancer. (Accepted for publication in Human Pathology).

KAPLAN COMPREHENSIVE CANCER CENTER



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activities at the Kaplan Comprehensive Cancer Center of NYU Medical Center.

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John Hill, Ph.D.
263-7689

Inhalation & Animal Care
Carroll Snyder, Ph.D.
(885)-5297

ARMY INVITES BREAST CANCER APPLICATIONS

The Department of the Army has issued a 1995 Broad Agency Announcement soliciting proposals related to breast cancer. The types of programs, available funds and deadline dates are indicated below.

Training and Recruitment - Up to \$14.7 million is allocated for training and recruitment in breast cancer to be funded as Predoctoral Fellowships, Postdoctoral Fellowships or Career Development Awards. The application submission deadline for training and recruitment projects is **September 8, 1995**.

Research Projects - Up to \$100 million is allocated for research projects which respond to any of the below six fundamental research issues (although any breast cancer related project will be considered).

- o What genetic alterations are involved in the origin and progression of breast cancer?
- o What are the changes in cellular and molecular functions that account for the development and progression of breast cancer?

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263-5341

Army Invites Breast Cancer Applications (Continued)

- o What is the role of endogenous or exogenous risk factors in the development of breast cancer as elucidated in population studies or other epidemiological investigations?
- o How can investigators use what is known about the genetic and cellular changes in breast cancer patients to improve detection, diagnosis, prevention, treatment and follow-up care?
- o What is the impact of risk, disease, treatment, and ongoing care on the psycho-social and clinical outcomes of breast cancer patients and their families?
- o How can the investigators define and identify techniques for delivering effective and cost-effective health care to all women and men to prevent, detect, diagnose, treat, and facilitate recovery from breast cancer?

Awards will be made in the categories of New Investigator awards, Innovative Developmental and Exploratory Awards (IDEA) and Other Investigator Initiated Awards. The deadline for submission of research project applications is **September 13, 1995**.

Mammography/Breast Imaging - Up to \$20 million is allocated for mammography/breast imaging projects under award categories Innovative Developmental and Exploratory Awards (IDEA); Other Investigator Initiated Awards; and Demonstration Projects. The deadline for submission of Mammography/Breast Imaging applications is **September 13, 1995**.

For further information and assistance please call Mr. Ira Goodman at extension 6703.

FACULTY HIGHLIGHTS

The following individual has been appointed a member of the Kaplan Comprehensive Cancer Center:

Dan Littman, M.D., Ph.D., Professor, Departments of Pathology and Microbiology and Molecular Pathogenesis Program Coordinator, Skirball Institute - Dr. Littman's interests lie in the area of molecular mechanisms of T cell activation and thymic development.

RESEARCH RESOURCES

Breast Tissue Resource for Research and Banking

The Breast Tissue Resource for Research and Banking was established in January, 1995 to provide investigators at NYU with neoplastic, preneoplastic and normal breast tissue. The Resource is funded as an infrastructure grant by the Department of the Army. To date 184 specimens have been accessioned. The emphasis of this effort is on the acquisition of precancerous breast lesions and early cancers. To obtain material and for further information contact Dr. Helen Feiner at extension 8826.

Precursor lesions of breast cancer are often clinically silent, are detected mammographically, and usually can not be seen with the naked eye in resected tissue. Because of the need to histologically define the most advanced lesion in each patient, pieces of tissue cannot be removed for research purposes from breast excisions for mammographically defined abnormalities. Instead, epithelial cells have been collected on multiple slides (imprints/touch or scrape preparations).

10-20 slides have been collected in each case. These were air dried and frozen at -70°C. Such samples are suitable for immunocytochemistry, immunofluorescence microscopy, in-situ hybridization and in-situ PCR. Cells can also be removed from slides for DNA extraction.

The inventory currently is as follows:

<u>Imprints/Scrape Preparations by Diagnosis</u>	<u># of Cases</u>
Non-proliferative fibrocystic change	13
Proliferative fibrocystic change	21
Atypical proliferative fibrocystic change	5

<u>Imprints/Scrape Preparations by Diagnosis</u>	<u># of Cases</u>
In situ lobular carcinoma	4
In situ ductal carcinoma	22
Early invasive lobular carcinoma	6
Early invasive ductal carcinoma	25
Fibroadenoma	10
Intraductal papilloma	4
Other	<u>6</u>
TOTAL	116

It is generally accepted that invasive breast cancers arise from histopathologically defined precursors: non-proliferative fibrocystic change (no increased risk), proliferative fibrocystic change (1.5 - 2 x increased risk), atypical proliferative fibrocystic change (4 x increased risk), lobular carcinoma in situ (10-11 x increased risk), and ductal carcinoma in situ (10 - 11 x increased risk, higher for high grade DCIS). The numbers refer to risk at 15 years of follow-up.

Standard banking of frozen pieces of tissue from established cancers and fibroadenomas has also been done. In such cases paired samples of normal and pathologic tissue are usually banked.

The inventory currently is as follows:

<u>Frozen Tissue by Diagnosis</u>	<u># of Cases</u>
Invasive ductal carcinoma	47
Invasive lobular carcinoma	10
Secondary carcinoma (lymph node)	3
Fibroadenoma	<u>8</u>
TOTAL	68*

(*paired sample of normal tissue available in 40 of the above cases).

The Breast Tissue Resource can also provide fresh breast cancer tissue and freshly prepared imprints to investigators prospectively.

NEW CLINICAL TRIALS

Phase II Study of SDZ PSC 833 in Combination with Paclitaxel in Patients with Paclitaxel-Refractory Advanced Ovarian Cancer. Investigator: Howard Hochster, M.D., beginning July 1, 1995.

Phase II Study of 9-20S-Amino-Camptothecin (9-AC) as Second Line Therapy in Advanced Ovarian Carcinoma. Investigator: Howard Hochster, M.D., beginning July 1, 1995.

Protocol 157-001 - A Prospective, Randomized, Multicenter Phase III Clinical Trial Comparing the Effects of Panorex 17-1 (A monoclonal antibody) Injection Plus 5-Fluorouracil Plus Levamisole Versus 5-Fluorouracil Plus Levamisole in Patients with Surgically Resected Stage III Carcinoma of the Colon. Investigator: Howard Hochster, M.D., beginning July 1, 1995.

PUBLICATIONS

(Kaplan Comprehensive Cancer Center members are noted by underscoring)

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